

REMARKS/ARGUMENTS

Claims 1-15 and 18-37 are pending in this application. Claims 1-13 and 32-33 are withdrawn. Claims 16-17 are canceled. Claim 31 has been amended to recite dependency on independent claim 14. No new matter has been added by the claim amendment. Thus, claims 14-15, 18-31, and 34-37 are presented for examination.

Claims 14, 15, 18-26, 28-31, and 34-37 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent Application Publication No. 2003/0008411 to Van Dam et al. (Van Dam) in view of U.S. Patent Application Publication No. 2002/037499 to Quake et al. (Quake).

Claim 27 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Van Dam in view of Quake as applied above, and further in view of U.S. Patent Application No. 2002/0102577 to Raillard et al. (Raillard).

Claim Rejections - 35 U.S.C. § 103

Independent claims 14 and 34 are drawn to methods of conducting a binding assay. The methods includes, among other elements, forming a plurality of looped flow channels. Each looped sample flow channel comprises a closed loop, and that sample solution is recirculated within the closed loop. The Examiner acknowledges that Van Dam "does not disclose the step of manipulating the valves to form a closed loop." (Office action at page 4). To make up for this deficiency in Van Dam, the Examiner relies on Quake. However, as explained below, the primary reference provides no suggestion or motivation to make the proposed combination. On the contrary, the combination suggested by the Examiner would decrease the utility of Van Dam's invention. As a result, Applicants respectfully submit that the proposed combination, rather than being based on desirability suggested by the prior art, is based on impermissible hindsight. Accordingly, based on MPEP 2142, the pending rejections should be withdrawn.

The Examiner is respectfully reminded that any suggestion to modify a reference must be found in the prior art, and cannot be based upon Applicants' own disclosure:

The tendency to resort to "hindsight" based upon applicant's disclosure is often difficult to avoid due to the very nature of the examination process. However, impermissible hindsight must be avoided and the legal

conclusion must be reached on the basis of the facts gleaned from the prior art.
(Emphasis added; MPEP 2142)

As discussed in the Amendment filed October 3, 2007, Van Dam discusses a linear or serpentine arrangement of flow channels that provide for a single-pass flow of reagents during the combinatorial synthesis of DNA N-mers. Van Dam discusses a method in which a set of reagents are sequentially flowed in a first direction (e.g., Step 1: Nucleic acids A/C/G/T sequentially flowing in the X-direction, Van Dam at paragraphs [0159] - [0165]). After this first step, "all 16 X-direction channels have been exposed to coupling reagents only once, i.e., the first base has been added to all 'rows' of the array." (Van Dam at paragraph [0164]). Then, the set of reagents are sequentially flowed in a second direction (e.g., Step 2: Nucleic acids A/C/G/T sequentially flowing in the Y-direction, Van Dam at paragraphs [0166] - [0173]). These two steps are repeated once in order to add all four bases to the compounds on the array. Thus, Van Dam, as illustrated in FIG. 12A, discusses a method in which the reagents enter at the injection sites (Inject-X or Inject-Y) on one side of the microfluidic device and exit at the waste sites (Waste-X or Waste-Y) on the opposite side of the microfluidic device.

In another embodiment, Van Dam describes a microfluidic device in which "[e]ach of the four channels in each elastomer has only one inlet and one outlet." These single pass flow channels are used so that "if the fluid reaches the outlet, it indicates that the fluid has reached every point in the channel." (Van Dam at paragraph [1028]). Thus, Van Dam only describes single-pass flow channels suitable for combinatorial synthesis. Therefore, Van Dam provides no suggestion that closed loop flow channels would be useful or beneficial to his invention. In other words, Van Dam provides no suggestion of the desirability of the combination proposed by the Examiner.

Moreover, if the linear flow channels of Van Dam were replaced with the closed loops of Quake, as suggested by the Examiner, then the concentration of reagent in the flow channel would decrease as function of time as the reagent was consumed. Such a concentration drop would increase the time required to perform synthesis. As a result, the utility of Van Dam's invention would be reduced, which is hardly a motivation to incorporate the combination suggested by the Examiner. Rather than suggesting the desirability of the combination, as required by MPEP 2143.01(I), the proposed combination, in fact, makes Van Dam's invention less desirable.

Thus, (1) the lack of any teaching or even suggestion in Van Dam of looped flow channels and (2) the fact that the proposed combination reduces the utility of Van Dam's invention, demonstrate that the desirability of the proposed combination is not found in the prior art as required by MPEP 2143.01(I). Rather these facts strongly indicate that the Examiner has taken the inventors' own disclosure as a "blueprint" for modifying Van Dam to defeat the patentability of the claims - "the essence of hindsight". In re Dembiczak 175 F.3d 994 (Fed. Cir. 1999) *citing* Interconnect Planning Corp. v. Feil, 227 U.S.P.Q. 543, 551 (Fed. Cir. 1985). For at least these reasons, claims 14 and 34 are in condition for allowance.

Claims 15 and 18-31, which depend from claim 14, are in condition for allowance, for at least the reasons discussed in relation to claim 14, as well as for the additional elements they recite.

Claims 35-37, which depend from claim 34, are in condition for allowance, for at least the reasons discussed in relation to claim 34, as well as for the additional elements they recite.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,

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